PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 173-204-WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/DK 03/00402	International filing date *(day/month/year)* 17.06.2003	Priority date *(day/month/year)* 26.06.2002
International Patent Classification (IPC) or both national classification and IPC C07D235/26		
Applicant POSEIDON PHARMACEUTICALS A/S et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
29.12.2003	03.08.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Hanisch, I Telephone No. +49 89 2399-7880

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/DK 03/00402

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-19	as originally filed

Claims, Numbers

1-8	as originally filed
9-23	received on 07.08.2003 with letter of 28.07.2003

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 19-23

   because:

   ☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-23
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-23
Industrial applicability (IA)	Yes:	Claims	1-18
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item III

Claims 19-23 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1 (iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject matter of these claims (Article 34(4)(a)(i)PCT).

Re Item V

Relevant prior art is provided by

(A) EP 0617023
(B) WO 0154771
(C) EP 0477819
(D) EP 0747354

Novelty

The overlapping parts of the current general formula (I) with the general formulae of (A) and (C) are considered to represent a novel selection therefrom. The novelty-destroying specific examples of (C) have been excluded from the present scope by means of a proviso. The current compounds appear to be novel vis-à-vis (B) on account of the "Hlg" substituent in the 5-position of the central benzimidazolinone ring and over (D) essentially on account of the said central ring itself.

Inventiv Step

The problem underlying the present application appears to be the provision of further benzimidazolinone derivatives which are better BK_{Ca} channel modulators.

(A)-(C) represent the most relevant prior art. (C) appears to be the closest prior art since it discloses not only a general formula widely overlapping with the current one but also specific examples which would fall within the scope of current formula (I) if not prevented from doing so by means of the proviso. However, a proviso cannot render an application inventive. A selection invention which is only novel vis-à-vis the closest prior art on account of a proviso is therefore seen as a mere generalisation of the excluded specific agent of the prior art. Consequently, an inventive step in the sense of Article 33(3) PCT may only be acknowledged if the current selection has any unexpected advantageous effect vis-à-vis the closest prior art compounds, which in this case appear to be those falling within the scope of the proviso. The said effect, however, may in such a case of very close prior art not automatically be attributed to the whole

general formula when shown for one single compound. Concerning the current application e.g. the four following comparative tests could be seen as an appropriate way of proving an inventive step: "Hlg" being chloro, bromo and iodo (current scope) compared to "Hlg" being fluoro ((C)) whereby R" always represents chloro, and a compound containing a substituent R" which represents anything but chloro (current scope) compared to another compound wherein R" represents chloro ((C)), whereby in both cases "Hlg" stands for fluoro. R' always has to be identical for each pair of comparison compounds. It should be noted that the comparative data on present pages 17 and 18 does not prove an inventive step since it does not relate to pairs of closest compounds because they differ in two substituents, not in only one. Thus, at present no unexpected improvement appears to be present so that an inventive step is preliminarily not acknowledged.

Industrial Applicability

For the assessment of present claims 19-23 on the question whether they are industrially applicable, no unified criteria exists in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.